

APPENDIX 9

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Attachment C

New hormone-replacer called better

Cincinnati-made drug said to have fewer side effects

By Tim Bonfield

The Cincinnati Enquirer

A hormone replacement therapy made in Cincinnati could help reduce side effects that cause many women to quit the medication.

The potential benefits come from the way the pill is made, rather than the medications it contains, say two

experts in women's health from Yale University and the University of Rochester who spoke at a recent seminar in Cincinnati on hormone replacement therapy.

"A major problem in hormone replacement therapy is discontinuance," said Dr. Philip Sarrel, a professor of obstetrics, gynecology and psychiatry at the Yale University School of Medicine.

About 40 percent of U.S. women ages 50 to 74 try hormone replacement therapy to control hot flashes and

other symptoms caused by menopause. However, about 25 percent of women quit taking the pills in the first month, and up to 80 percent quit within two years.

Dr. Sarrel said women can get better control with Cenestin, a still-new hormone replacement drug made by Duramed Pharmaceuticals Inc., than with the market-leading product, Premarin, made by Wyeth-Ayerst Pharmaceuticals.

Blood test data presented at the seminar indicate that

Premarin pills can release anywhere from 15 percent to 60 percent of their estrogen ingredients within two hours. But Cenestin consistently releases 30 percent to 40 percent of its estrogens during that time.

"I think (the difference in

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dose consistency) is clinically significant," Dr. Sarrel said.

The pill debate is important because millions of American women are affected by menopause, and more will be as the baby boom generation ages.

An estimated 20 million women will reach menopause in the next decade. Already a \$2.5 billion industry, analysts forecast the hormone replacement market to expand to nearly \$4 billion by 2005.

But hormone replacement also has been a controversial topic.

Scientists continue to debate whether hormone therapy can prevent heart disease or increase the risk. Animal-rights groups have criticized the use of pregnant horses as the most common source of hormone therapy medications. Women who take hormone replacement therapy also can increase their risk of breast and uterine cancer.

Presentations in Cincinnati focused on technical issues.

"Premarin was state-of-the-art in the 1940s, and it is still the most widely used. The problem is that this is an old product," said Dr. Henry Hess, an associate clinical professor of obstetrics and gynecology at the University of Rochester School of Medicine.

Premarin was introduced in 1942. Its active ingredients come from the urine of pregnant mares, and the pills are coated with pharmaceutical shellac, a substance derived from beetle husks.

In part because Premarin was approved so long ago, the amount of hormone in the pills is allowed to range more widely and release less consistently than medications seeking FDA approval today, Dr. Hess said. Cenestin hit the market in March 1999 after Durand spent years seeking approval from the U.S. Food and Drug Administration. Its active ingredients are derived from yam and soybean plants.

Cenestin differs from Premarin because its ingredients are coated with polymers during manufacture. As the Cenestin pill moves through the intestine, the polymers break up, releasing the hormones at a more even, steady pace than Premarin.

In theory, a more consistent medication can help avoid ups and downs in hormone levels that doctors say can cause problems such as breast tenderness, mid-cycle bleeding, migraines, mood swings and continued hot flashes, Dr. Hess said.

In fact, Dr. Hess said his practice group has treated more than 200 women with Cenestin and many report "significant improvement" in reducing unwanted problems.

However, such information is anecdotal. Some doctors say they are still waiting for controlled head-to-head studies comparing side effects among users of Premarin and Cenestin. Those studies have not been completed.

"With a more predictable release, you are likely to get a more predictable biological response. But is there enough of a difference to show a clinical effect (such as reduced side effects in women)? I don't think anyone can say, because there haven't been any studies," said Dr. James Liu, director of the University of Cincinnati's division of reproductive endocrinology.

Dr. Liu said he often prescribes Cenestin for women starting hormone replacement therapy, but for women already taking Premarin he hasn't seen enough data to suggest they should switch.

"Both are very good products and there is no real difference in pricing," Dr. Liu said.

Premarin's manufacturer, Wyeth-Ayerst, said the dose dissolution information presented last week did not prove anything.

"The overall body of scientific evidence does not support claims that any other product delivers a more effective dose of estrogen for women using HRT than Premarin," said spokesman Doug Petkus.

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